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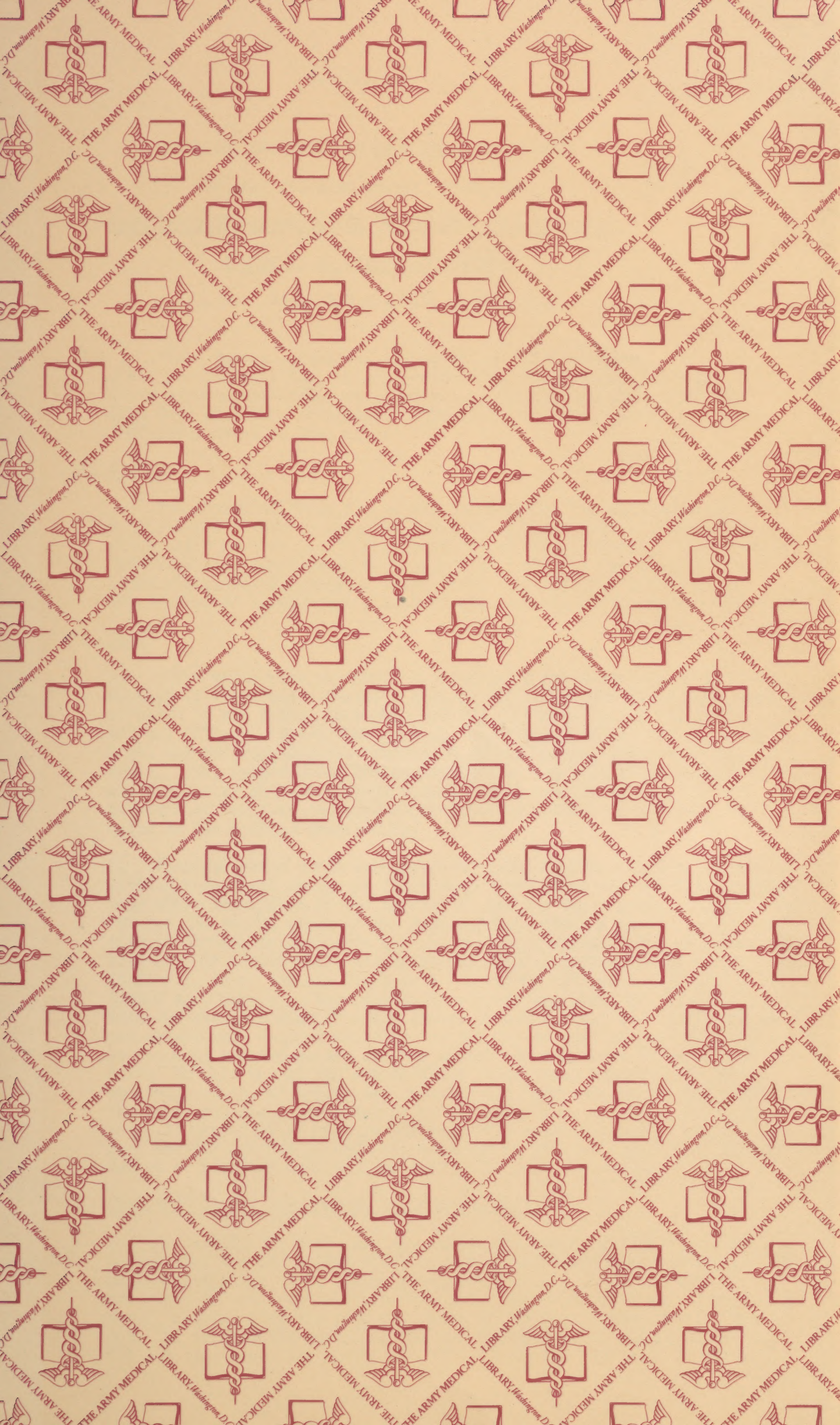
EFFECT OF SULPHADIAZINE PROPHYLAXIS ON RESPIRATORY INFECTION OF SERVING SOLDIERS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R E P O R T

to

ASSOCIATE COMMITTEE ON ARMY MEDICAL RESEARCH

National Research Council of Canada

THE EFFECT OF SULPHADIAZINE PROPHYLAXIS ON RESPIRATORY INFECTION OF SERVING SOLDIERS

Col. F.P. Lloyd O.B.E., V.D., R.C.A.M.C.

I. Field trials concerning the effect of Sulphadiazine, given prophylactically, on the incidence of Respiratory Infection among serving soldiers were commenced in Camp Borden Command on the 24th Oct. 1944 and terminated on the 15th Apr. 1945. (Auth. H.Q. 54-27-7-340-1 dated 21 Sep. 44).

II. OBJECT

The object of these trials was to determine the problems and difficulties of such a measure, using the minimum dose of Sulphadiazine which under service conditions would reduce the incidence of Respiratory Infection to a significant degree, and to determine the results that could reasonably be expected there from. The test was not to be of the 'hothouse' variety but practical and workable under all conditions.

III. PLAN

1. Seven units were selected representing a cross section of the Army. To each of these was attached a trained NCO called the "Test NCO", who reported to the Senior Test NCO (W.O.II) in the office of the Senior Medical Officer. These NCOs were all experienced in the Quartermaster's Dept. and had considerable experience in the Medical Inspection Rooms of Units. They worked under the supervision of the Unit Medical Officers and the Senior Hygiene Officer respectively, the latter advising the Director of the test and giving constant supervision as he visited the units on his routine inspections.

2. From the seven units were selected 5,000 healthy soldiers who were divided into equal groups in their respective units and the huts in which they slept identified by the letter "A" for the first group and the letter "B" for the second group as the case may be. Under a carefully prepared plan of control in each unit all the men who slept in "A" huts were issued with one "A" tablet each morning at roll call immediately after awakening. Similarly, every man who slept in a hut marked "B" was issued with a "B" tablet each morning. Accurate daily records were kept of every man under test who reported sick from any cause. A man was considered sick if he was absent from duty or training for one day or more because of illness and he was only counted as one case no matter how many days he was absent from duty. In this way at the commencement of the test there were 2,500 men who received an "A" tablet each morning and 2,500 men living under exactly the same conditions who received a "B" tablet each morning. It was not known by those taking part in the test what these tablets contained. In each hut "A" and "B" groups were selected so that soldiers doing similar duties or training were divided equally between the groups.

PROCEDURE IN HUT AND COMPANY OR SQUADRON OFFICE

3. At reveille as each name was called the NCO in charge of the hut handed that man one tablet which he was asked to swallow. If he objected no compulsion was used. If he persisted the Coy. (Squad. etc) Commander was asked to move him to a non-test hut. This was not always done. When a man reported sick his name was taken by the Coy. (Squad. etc) Orderly Sgt. who entered the number of his hut and whether it was in an "A" or "B" hut on a specially marked MFM 292. Since the test huts in any Coy.

were well known, the Orderly Sergeant knew at once the correctness of this record.

4. PROCEDURE AT THE UNIT MEDICAL INSPECTION ROOM

The special Test NCO issued to each Test Hut NCO i/c every three days a bottle of tablets marked with a plain "A" (Red) or "B" (Black) sufficient for his particular hut. Tablets were counted and signed for and a record kept. Each Hut NCO got only one kind of tablets. At the morning sick parade the Medical Officer examined each soldier, asked him what hut he slept in, whether he was taking tablets and if so what kind. He checked the man's answers with the 292 when he entered his diagnosis on that form. If the man was suffering from a Respiratory Infection the Medical Officer put a plain cross before and after his diagnosis, thus (X Coryza X).

5. The Test NCO then reviewed all 292's. If he found Respiratory Infection which had not been marked by the Medical Officer he immediately drew the fact to that Officer's attention and if a mistake had occurred it was corrected at once. Having assured himself on this point he then proceeded to the hut of every man who was in the test whom the M.O. had marked as having Respiratory Infection, and the hut orderly verified the correctness of the men's statements. If possible he saw the man and asked him whether or not he had taken the tablets, and questioned the Hut NCO as to whether he had given the tablets. When every step had been double checked the Test NCO prepared a return known as "The White Form" which consolidated the following information for the Unit: Name, Number, Hut Number, Provisional Diagnosis and Final Diagnosis of all those having a a Respiratory Infection. Those in "A" Huts and who had taken "A" tablets who had been either excused duty for one or more days or sent to hospital were entered on the upper half of the form; on the lower half of the form similarly a consolidation was made of all those who slept in "B" Huts and had taken "B" tablets. These White Forms were prepared serially throughout the experiment and sent daily to Camp HQs. Nil reports being required, the serial number of the form coincided with the day of the test; serial 99 gave the situation on the 99th day and so on.

6. HOSPITAL RETURNS

The special Test NCO also examined all men in the unit who returned from hospital each day. If any man had been previously sent to hospital while under test the NCO prepared a "Blue Form" also serially numbered in which was reported the man's name, number, hut number and "A" or "B" with the hospital diagnosis and the number of days in hospital. The serial number of the white form on which he had originally been reported to HQs was carefully checked and entered. This Blue Form and the White Form for that day were securely stapled together and sent to Camp Headquarters.

7. PROCEDURE AT COMMAND HEADQUARTERS

A specially trained CQMS received the reports from all units daily. Under the direction of the Senior Hygiene Officer this NCO reviewed each return and compared the data thereon with the copies of the original 292's made at the time the man reported sick. If all was correct he then compared the hospital diagnosis with the original diagnosis as made by the Unit Medical Officer. If the hospital diagnosis was not one of Respiratory Disease Infection the case was eliminated from the record. If the diagnosis was changed the fact was noted as the Final Diagnosis on the original White Form. In this manner it was possible to make certain that every case of Respiratory illness among soldiers under test was correctly reported and correctly recorded.

8. All Medical Officers and M.I.R. NCOs were warned to watch for reactions, and to be especially vigilant with every case of illness no matter how slight and to see that it was investigated. With the exception of the Director of the test and the Senior Hygiene Officer no one knew the composition of either the "A" tablets or the "B" tablets.

9. CONDITIONS IN UNITS

In most units and in all training units there is a constant flow of men in and out. These conditions were accepted because, though the segregation of men under test would have produced much more impressive results, it is also true that such results would hot have been reduplicated in a practical application of the method under service conditions. It is estimated that 75% of the men under test changed three times over or more during the five and one half months it continued. It follows that many of the men after having taken the tablets for a month or six weeks passed out of the test to be replaced by 'raw men' who had had no prophylaxis. The subsequent favourable record of the "lost" men was replaced by the higher rate of the 'raw' men for the 15 to 20 days necessary to immunize them. This higher rate is included in the record of the treated group.

10. With regard to the numbers of men involved, the intention was to have 5,000 at all times under test. It soon became impossible to obtain this number of men without interfering with training. As a result daily counts were made and an average of 3,994 was maintained for the five and a half months of the test. Of these 2020 were "A" Huts and 1974 were in "B" Huts. This is compensated for by expressing the results in rates per thousand or rates per thousand per annum.

11. TIME OF TEST

It was visualized when the test was authorized that there would be a relatively high incidence of Respiratory Infection because of the winter weather. Fortunately for the Army but unfortunately for our results the expected increase in R.I. did not occur. The increase of patients in hospital (CBMH) during January, February and March 1945 was only 100 daily over the average summer count for the last three years-an increase of only 25%. For this reason the results obtained must be viewed in an entirely different light to those obtained in the United States at the height of a pandemic of Respiratory Disease. In fact the significance of these results is enhanced by the lack of an epidemic.

12. ATTITUDE OF THE MEN

The Commanding Officers having been interviewed by the Director of the Test and their cooperation assured, the Company Officers, under the CO's orders, explained to their own men the reasons for and plan of the test. At first a relatively high percentage of the men refused the tablets without explanation. It was then discovered that the word had got around, due possibly to the publicity given to V.D. Prevention, that the tablets contained saltpetre or some such substance to be given to soldiers surreptitiously to reduce V.D. To meet this it was found necessary to post a notice in each hut putting the case as fairly and forcibly as possible and to include a frank statement to the effect that these tablets had nothing whatever to do with V.D. Control. (Copy att'd Appendix "B"). This notice was signed by the Director as S.M.O. Such efforts had considerable effect and the number of men who swallowed the tablets materially increased.

IV. RESULTS

1. General

In spite of the faithful cooperation of all concerned there was still, as there always will be, a proportion of the men who did not actually take the tablets. Every effort was therefore made to arrive at a figure which would enable a correction to be made to allow for this important factor. However, it is felt that this correction should not be applied to the results except for purposes of scientific analysis. It is altogether unlikely that an instrument of this kind would be used except in the emergency of a threatened epidemic or a pandemic. Since when this test was made it was a healthy year with little increased incidence of Respiratory Infection present, the probable results in the face of an epidemic might reasonably be doubled. In this case results obtained in Camp Borden under the conditions which have been noted almost exactly duplicated the results obtained in the United States during the epidemics of 1943 and 1944.

2. REPORTS BY UNITS

The results are reported both as actual cases and as rates per thousand per annum. Since the latter alone gives the true comparative picture it will form the basis of discussion. Tables I for "A" Huts and II for "B" Huts give a breakdown by units of cases as they occurred, reported bi-monthly and divided into those excused duty (Ex) and admitted to hospital (Hp).

Cases "A" Huts	Ex 252	Hp 150	Total 402
Cased "B" Huts	Ex 149	Hp 109	Total 258
A-B	103	41	144

3. DAILY COUNTS AND RATES

A daily count of men under test arranged in bi-monthly groups with a consolidation of cases and rates per thousand per annum calculated therefrom is presented in Table III. The first period Nov 1-15 is discarded for the record due to the difficulties in taking tablets referred to in Sec III, para 12 above. In Chart I these rates are graphically represented. These points should be noted.

I. The "B" Hut men start the test with double the illness rate of the "A"s.

II. In two weeks of prophylaxis the positions are reversed. "A" has risen from 108 to 314 while "B" has fallen from 224 to 204.

III. Favourable progress continued till 31 Dec when "B"s are 50% of "A".

IV. The effect of a general laxity in taking tablets during Xmas and New Year wiped out the favourable results to 8% by the 15 January.

V. From that time on favourable results increase until the warm weather of 15 Mar-15 Apr reduces the rate to "A"-224 and "B" 154, still a significant difference.

4. MAN DAS SAVED

A consideration of the tables shows that there were 144 men saved from illness by the prophylaxis. This works out at thirty five percent of those who were ill or a reduction of illness by 164 per thousand healthy men per annum. The average time lost while ill for each "A" tablet man was 5.6 days. The man days saved per year per thousand men is therefore 9.184 man days.

5. BREAKDOWN BY DISEASES

Table IV shows the breakdown by the various types of Respiratory Disease. The only one not materially decreased by the prophylaxis was bronchitis. No explanation can be offered for this fact.

6. REACTIONS

During the five and a half months that Sulphadiazine was administered there were three cases of dermal reaction only of which one was doubtful. Though they were admitted to hospital none were actually ill.

The first case B-468006 Tpr Atkinson, W.H. developed an itchy rash of the 'scarlet fever' type on 11 Dec 44. He is said to have been taking "B" tablets for three weeks--but his urine was neg. for sulpha. He had also been taking service vitamin tablets (other cases have occurred with a similar rash definitely from these tablets). His rash cleared in 36 hours and he returned to duty. Doubtful case.

The Second case on 15 Jan 45 - B-52397 Cpl. Morris, P. developed a generalized rash of the Erythema Multiforme type over the areas of the skin that are exposed to the sun when wearing summer clothing (shorts and shirts). He had been taking "B" tablets for six weeks and his urine was positive for sulpha. Rash lasted seven days with no subsequent ill effects.

The third case on 19 Feb 45 - B-166285 Pte Truesdell, F.R. developed a rash of the Rubella type. His urine was positive and the rash latent 36 hours.

Counting three cases gives a rate of 1.5 per thousand for 5½ mons.

7. PERCENTAGE OF TEST MEN TAKING TABLETS

Difficulty was experienced in getting men under test to actually take the tablets offered. In spite of the measures adopted to persuade them a certain number did not always accept the tablets and others accepted them but did not swallow them. A careful check was made of this point in all units and from the counts made throughout it is estimated that 53% of the men actually took the tablets while 47% did not actually swallow them.

It might therefore be argued that if a reduction in Respiratory Disease amounting to 35% took place with only 53% of the men under test actually swallowing the tablets, then if 100% had swallowed them there would have been a reduction of 66% in Respiratory Disease. Calculated in rates per thousand per annum of healthy men this would mean a reduction in illness of 309 per M.

V. SUMMARY

Purpose

To obtain familiarity with the administrative problems arising out of a large scale prophylactic measure. To test the possibility of rapidly putting such a measure into effect on the threat of an epidemic and to test its effectiveness under Canadian conditions. The test was to coincide with the 'epidemic period' of Respiratory Diseases.

Conclusions

1. No epidemic of Respiratory Infection occurred during the period of the test (See Chart #3 for comparisons) therefore the results are the most conservative that can be expected.

2. Only 47% of the men under test actually swallowed the tablets, no compulsion being used. This fact constitutes a problem in the event of the use of the measure to check an epidemic.

3. Reactions to the drug were mild and negligible in number, 1.5 per thousand over 5½ months.

4. The test showed a reduction in Respiratory Disease of 35% (or 164 per M. per annum) due to the prophylaxis. This is likely to be doubled under epidemic conditions and moderate compulsion.

5. The measure can be carried out by the normal administrative organization of any unit (Regt. or Bn.) having a Medical Officer and staff attached. The medical supervision must be efficient and strict.

6. The plan can be put into effect in 24 hours provided the necessary tablets are available.

7. It may take 14 to 21 days before maximum effect is apparent if no epidemic exists.

8. A special directive is required to point out the salient features (attitude of men, necessity must be explained, reactions provided for etc.).

SULPHADIAZINE PROPHYLAXIS TEST

Ex - Excused Duty
Hp - Hospital

Table I

Number of Cases Excused Duty and Admitted to Hospital

"A" TABLETS (Placebo)

Units	A-19		A-22		No.1 TR		No.2 TR		No.3 TR		TSR		A-10		Total		Total
Dates	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Both
*Nov 1-15	1	-	-	2	2	-	-	-	2	-	1	1	-	-	6	3	9
Nov 16-30	1	1	2	3	2	4	-	-	3	1	3	-	8	2	19	11	30
Dec 1-15	1	-	6	1	-	4	2	2	7	-	-	-	11	5	27	12	39
Dec 16-31	-	-	7	-	6	3	2	-	13	-	1	-	5	3	34	6	40
Jan 1-15	2	-	-	2	8	6	6	2	4	1	4	-	5	2	29	13	42
Jan 16-31	8	-	4	-	2	2	11	4	7	-	-	-	8	5	40	11	51
Feb 1-15	1	1	3	-	2	6	6	7	6	-	1	1	9	10	28	25	53
Feb 16-28	1	-	1	1	8	10	-	-	5	7	1	-	7	5	23	23	46
Mar 1-15	2	-	1	-	1	5	2	15	8	1	1	-	4	8	19	29	48
Mar 16-31	-	-	1	-	3	7	14	5	3	-	-	1	-	2	21	15	36
Apr 1-15	2	1	-	-	7	2	3	2	-	-	-	-	-	-	12	5	17
TOTAL	19	3	25	9	41	49	46	37	58	10	12	3	57	42	258	153	411
														Record Total	252	150	402

*For purposes of this record the count will begin with Nov 16-30, the period Nov 1-15 being discarded.

Ex - Excused Duty
Hp - Hospital

Table II

SULPHADIAZINE PROPHYLAXIS TEST

Number of Cases Excused Duty and Admitted to Hospital

"B" TABLETS (.5 gms Sulphadiazine)

Units	A-19		A-22		No.1 TR		No.2 TR		No.3 TR		TSR		A-10		Total		Total
Dates	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Ex	Hp	Both
*Nov 1-15	-	-	1	1	1	1	-	1	1	1	4	1	5	2	12	7	19
Nov 16-30	-	1	2	2	4	1	1	-	2	-	2	1	2	1	13	6	19
Dec 1-15	1	1	3	8	-	2	-	1	1	-	2	1	1	2	8	15	23
Dec 16-31	-	-	2	1	2	1	1	1	-	-	1	2	5	1	11	6	17
Jan 1-15	4	-	-	3	9	6	5	3	4	-	1	1	4	1	27	14	41
Jan 16-31	5	-	1	1	5	3	5	3	-	2	3	-	5	2	24	11	35
Feb 1-15	2	-	1	1	-	3	1	1	8	1	3	-	3	6	18	12	30
Feb 16-28	-	-	1	1	2	2	5	1	6	2	-	-	3	4	17	10	27
Mar 1-15	1	-	-	-	5	3	2	5	7	1	1	1	1	7	17	17	34
Mar 16-31	-	-	-	-	1	5	2	2	-	2	2	1	2	4	7	14	21
Apr 1-15	1	-	-	-	3	2	-	1	-	-	3	-	-	1	7	4	11
TOTAL	14	2	11	18	32	29	22	19	29	9	22	8	31	31	161	116	277
														Record Total	149	109	258

*For purposes of this record the count will begin with Nov 16-30, the period Nov 1-15 being discarded.

SULPHADIAZINE PROPHYLAXIS TEST

Table III

Daily Average Count of Men in "A" and "B" Huts

Cases of Respiratory Illness and Rates per Thousand per Annum.

Period	"A" Huts with "A" Tablets			"B" Huts with "B" Tablets		
	Average Daily Count	Cases Resp. Ill.	Rate Per M.	Average Daily Count	Cases Resp. Ill.	Rate Per M.
*Nov 1-15	2001	9	108	2037	19	224
Nov 16-30	2268	30	313	2231	19	204
Dec 1-15	2260	39	414	2118	23	261
Dec 16-31	2257	40	425	2069	17	197
Jan 1-15	1949	42	517	2104	41	468
Jan 16-31	2143	51	571	2075	35	405
Feb 1-15	2131	53	597	1813	30	397
Feb 16-28	1876	46	588	1880	27	345
Mar 1-15	1776	48	649	1813	34	450
Mar 16-31	1735	36	498	1809	21	279
Apr 1-15	1825	17	224	1712	11	154
Total for Record	2020	402	473	1974	258	314

*Discarded for Record purposes

Table IV

CASES OF RESPIRATORY ILLNESS AMONG SOLDIERS TAKING

"A" or "B" TABLETS

ARRANGED BY DISEASES SHOWING DECREASE DUE TO PROPHYLAXIS

DISEASE	"A" Tablets	"B" Tablets	Effect using "A" as Standard			
			Increased		Decreased	
			Cases	%	Cases	%
Measles	1	1	-	-	-	-
Chicken Pox	2	-	-	-	2	-
Mumps	32	23	-	-	9	22%
German Measles	2	2	-	-	-	-
Scarlet Fever	-	1	1	-	-	-
Pneumonia	13	5	-	-	8	61%
Influenza U.R.I.	88	46	-	-	42	48%
Tonsilitis	24	26	2	8%	-	-
Pharyngitis	101	60	-	-	41	41%
Laryngitis	13	5	-	-	8	62%
Bronchitis	23	33	10	43%	-	-
Tracheitis	11	3	-	-	8	73%
Septic Sore Throat	17	8	-	-	9	53%
Otitis Media	5	3	-	-	2	-
Pleurisy	3	1	-	-	2	-
Coryza	64	42	-	-	22	34%
Sinusitis	3	6	3	-	-	-
TOTAL	402	258	-	-	144	35.8%

Under test 5,000 Men

Duration of Prophylaxis 5 Mos
Duration of Record $4\frac{1}{2}$ Mos

Remarks:

Less than 10 cases not given in percent.

PROPHYLACTIC SULFADIAZINE TEST, CAMP BOWIE -- Rates per THOUSAND Men

CHART 2

Respiratory Infection in Test Huts, Cases, with Rates

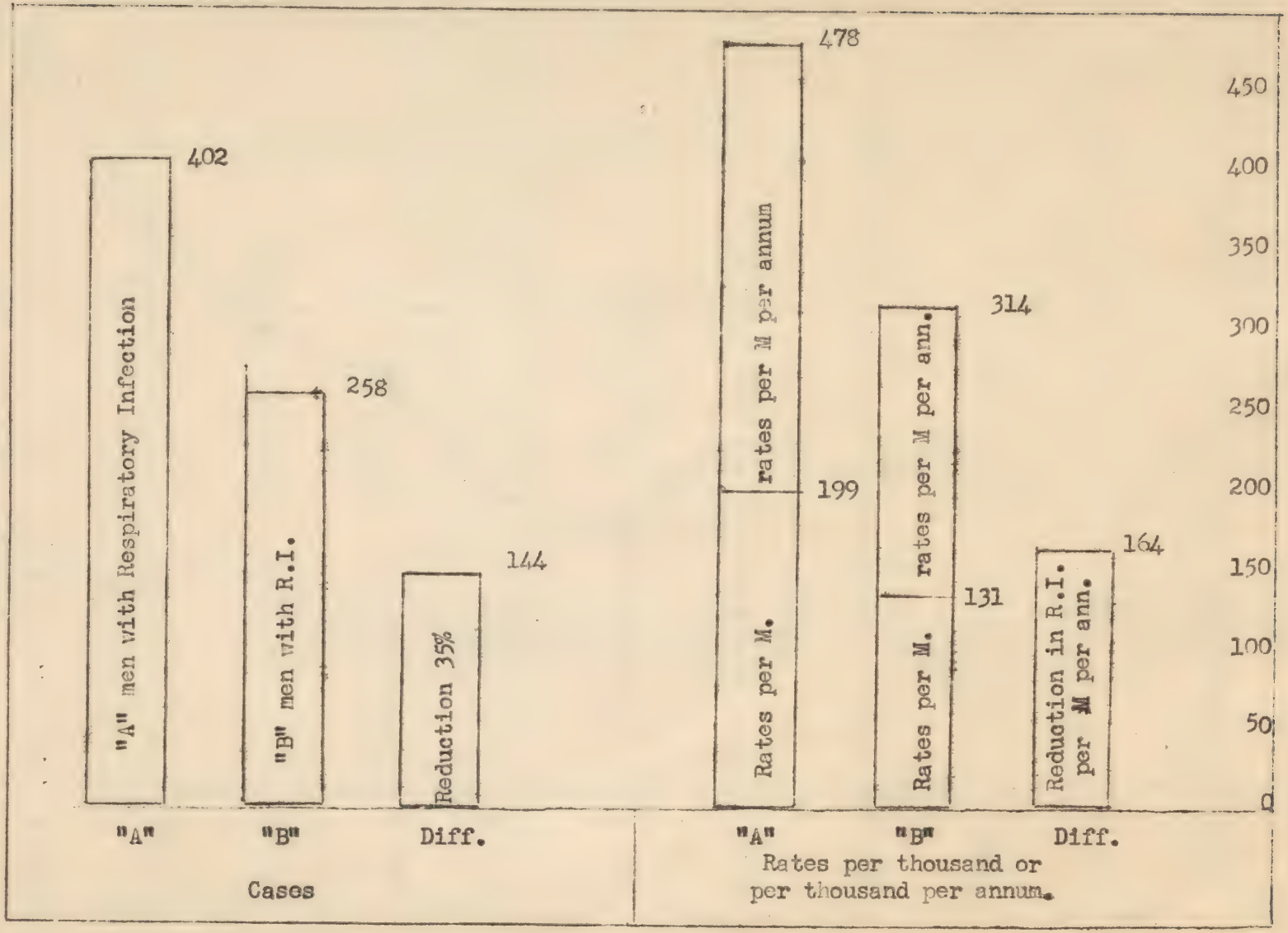
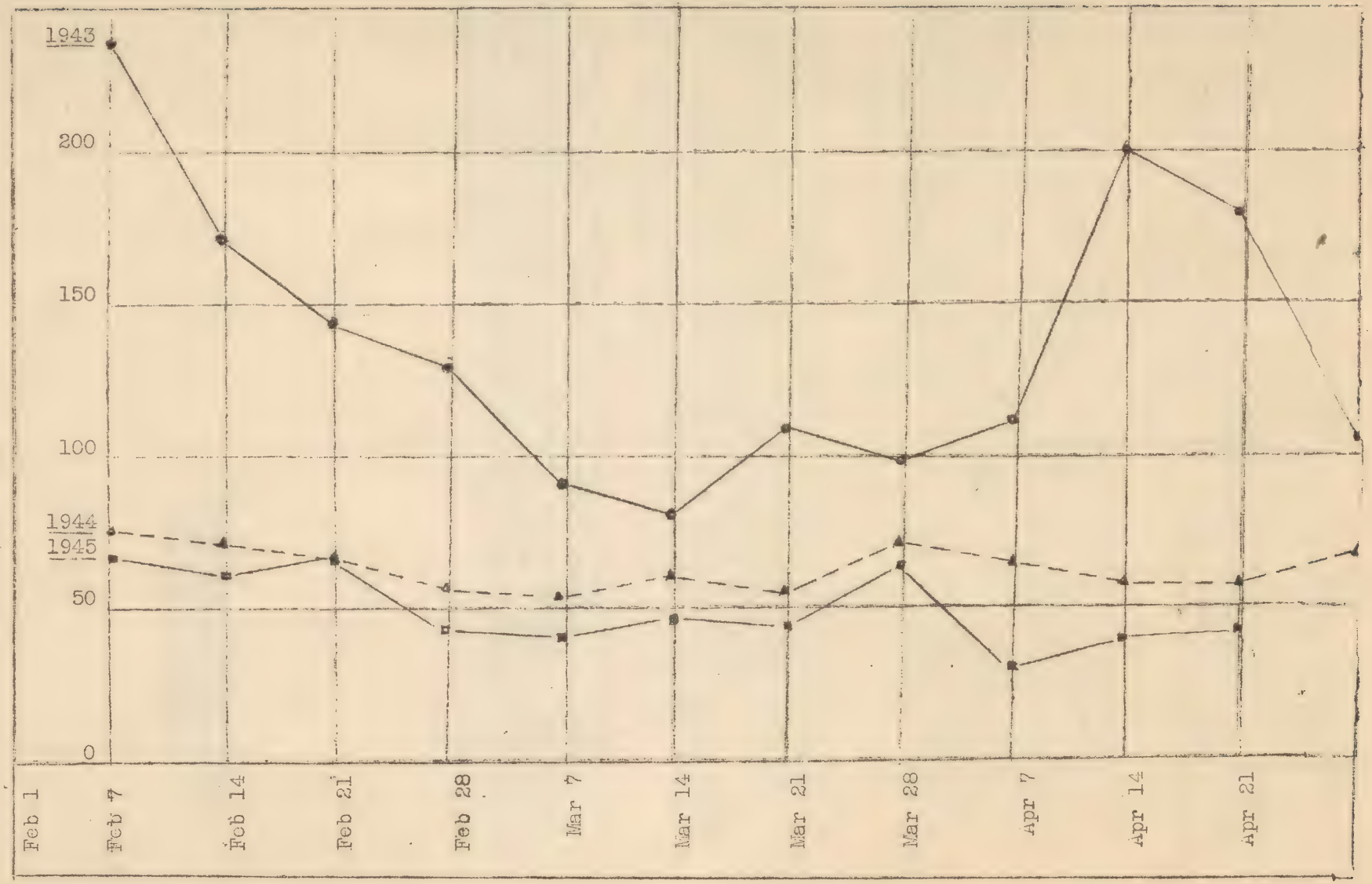


Chart 3

Weekly Admissions C.B.E.H. Respiratory Disease



Appendix B

THIS IS A "B" HUT

It is most important for the health of the Army (Navy and Air Force also) for the Medical authorities to know exactly the best way of preventing disease, because prevention is always better than cure. Respiratory diseases such as sore throat, tonsillitis, bronchitis, pneumonia, etc. if unchecked often leads to such conditions as rheumatism, scarlet fever, heart trouble and kidney trouble etc. It has been found that if respiratory diseases can be prevented, a man is much more likely to remain healthy and free of such chronic conditions.

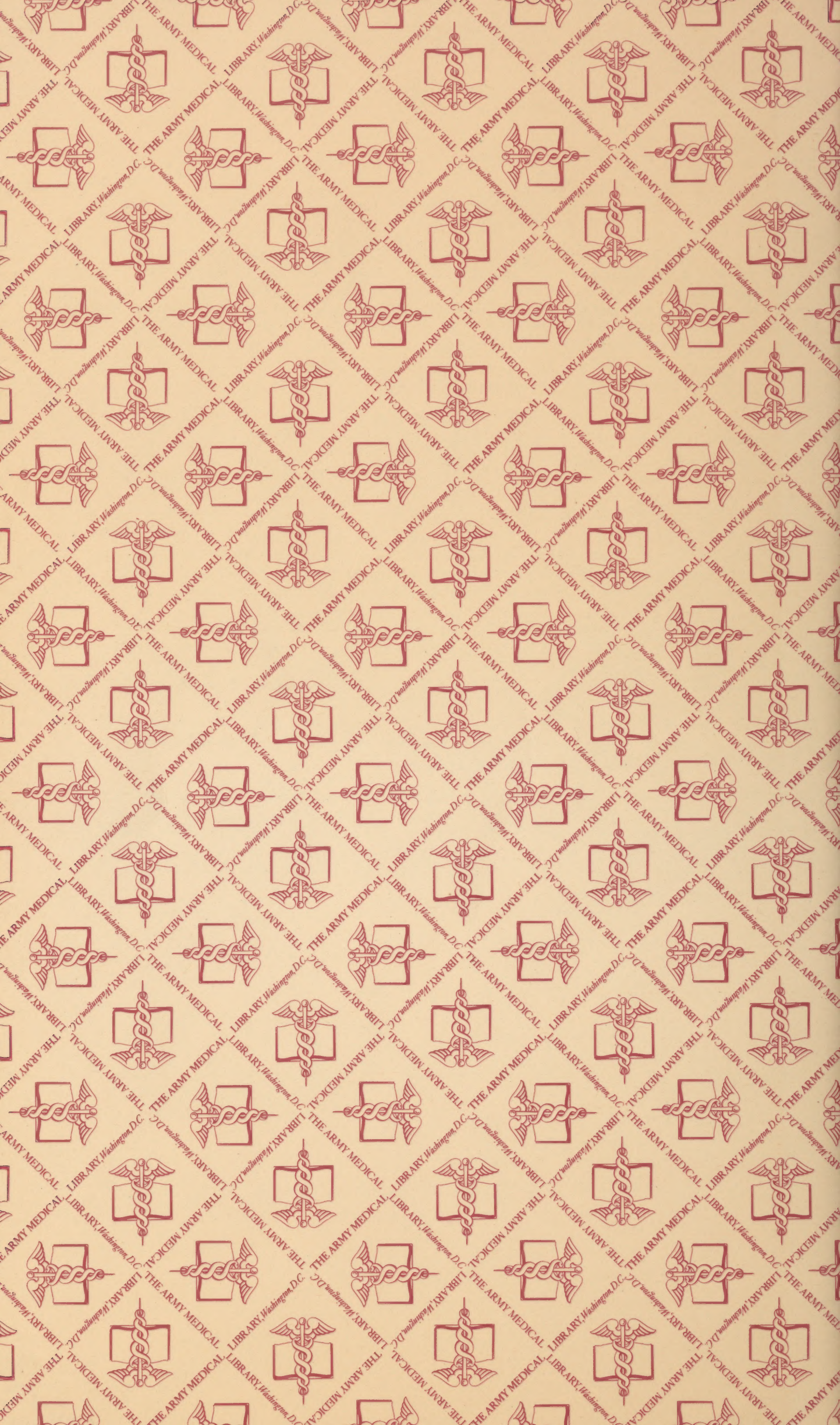
2. It is known that infected dust causes respiratory diseases. Valuable information was produced by a blanket test in Camp Borden in recent months. You are now being asked to help in making these tests more complete by taking a small tablet called a "B" tablet each morning when you get up. The purpose of this tablet is to prevent germs that you may have breathed in either during the night or from a theatre etc, developing in your system, causing respiratory disease. This tablet will not effect you in any other way any more than an aspirin would. (This statement is made by the medical authorities to make it plain that this test has no connection with venereal disease prevention.)

3. Careful records will be kept by the Medical Officer of every case of illness and if you will cooperate by doing as you are requested, information of the utmost value for the prevention of diseases such as scarlet fever, rheumatism, arthritis, brain fever, kidney disease, etc. can be gained. The results for the future health of the people of Canada are so important that you are urged to do your part in making this test a complete success. Remember that YOU may be able to prevent some other person from becoming a cripple.

4. Every war has produced great advances in medicine because medical services have been able to produce new and better remedies. So true is this, that in the end, more lives may be saved by the improved treatments, than were lost during the war. Camp Borden has already done excellent work in this regard. You can be of further help in a most important way by taking part in this test.

18 Oct 44

(F.P. Lloyd) Col., RCAMC,
Senior Medical Officer,
Camp Borden Command.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